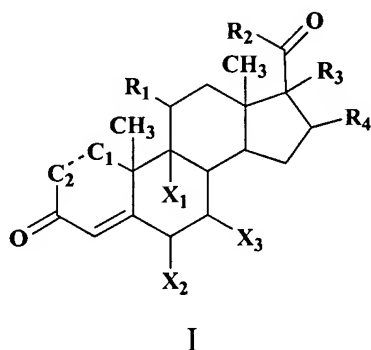


1. A corticosteroid conjugate comprising a corticosteroid attached to a group that is either a bulky group of greater than 400 daltons or a charged group of less than 400 daltons, wherein said corticosteroid conjugate has anti-inflammatory activity *in vivo* and reduced activity in the central nervous system in comparison to said corticosteroid without said group.

2. The corticosteroid conjugate of claim 1, wherein said corticosteroid is covalently attached via a linker to said group.

3. The corticosteroid conjugate of claim 2 having formula I:



wherein

the bond between C<sub>1</sub> and C<sub>2</sub> is a double or a single bond;

X<sub>1</sub> represents -H or a halogen atom;

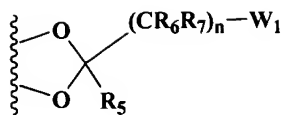
X<sub>2</sub> represents -H, -CH<sub>3</sub>, or a halogen atom;

X<sub>3</sub> represents -H or a halogen atom;

R<sub>1</sub> represents =O or -OH;

R<sub>2</sub> represents -CH<sub>3</sub>, -SCH<sub>2</sub>F, -CH<sub>2</sub>Cl, -CH<sub>2</sub>-G, -CH<sub>2</sub>OH, -CH<sub>2</sub>O-P(O)(O<sup>-</sup>)<sub>2</sub>, CH<sub>2</sub>O-acyl, -CH<sub>2</sub>NH-G<sup>1</sup>, -CH<sub>2</sub>S-G<sup>1</sup>, or -CH<sub>2</sub>O-G<sup>1</sup>;

R<sub>3</sub> and R<sub>4</sub> each, independently, represents -H, C<sub>1-10</sub> alkyl, -OH, -O-acyl, -O-G<sup>1</sup>, or R<sub>3</sub> and R<sub>4</sub> combine to form a cyclic acetal of formula II wherein:



II

n is an integer from 0 to 6;

R<sub>5</sub>, R<sub>6</sub>, and R<sub>7</sub> each, independently, represents -H or C<sub>1-10</sub> alkyl;

W<sub>1</sub> represents -H, -CH<sub>3</sub>, -G<sup>1</sup>, -NR<sub>8</sub>-G<sup>1</sup>, -NH-NH-G<sup>1</sup>, -O-G<sup>1</sup>, -S-G<sup>1</sup>, -C(O)-G<sup>1</sup>, or -C(S)-G<sup>1</sup>;

R<sub>8</sub> represents -H, C<sub>1-10</sub> alkyl or C<sub>5-10</sub> aryl; and

G<sup>1</sup> is a bond between said corticosteroid and said linker.

4. The corticosteroid conjugate of claim 3, wherein said linker is described by formula III:



III

wherein

G<sup>1</sup> is a bond between said corticosteroid and said linker;

G<sup>2</sup> is a bond between said linker and said bulky group or between said linker and said charged group;

Z<sup>1</sup>, Z<sup>2</sup>, Z<sup>3</sup>, and Z<sup>4</sup> each, independently, is selected from O, S, and NR<sub>11</sub>;

R<sub>11</sub> is hydrogen or a C<sub>1-10</sub> alkyl group;

Y<sup>1</sup> and Y<sup>2</sup> are each, independently, selected from carbonyl, thiocarbonyl, sulphonyl, or phosphoryl;

o, p, s, t, u, and v are each, independently, 0 or 1; and

R<sub>10</sub> is a C<sub>1-10</sub> alkyl, a linear or branched heteroalkyl of 1 to 10 atoms, a linear or branched C<sub>2-10</sub> alkene, a linear or branched C<sub>2-10</sub> alkyne, a C<sub>5-10</sub> aryl, a cyclic system of 3 to 10 atoms, -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>q</sub>CH<sub>2</sub>CH<sub>2</sub>- in which q is

an integer of 1 to 4, or a chemical bond linking  $G^1-(Z^1)_o-(Y^1)_u-(Z^2)_s-$  to  $-(Z^3)_t-(Y^2)_v-(Z^4)_p-G^2$ .

5. The corticosteroid conjugate of claim 1, wherein said bulky group comprises a naturally occurring polymer or a synthetic polymer.
6. The corticosteroid conjugate of claim 5, wherein said naturally occurring polymer is a glycoprotein, a polypeptide, or a polysaccharide.
7. The corticosteroid conjugate of claim 5, wherein said bulky group comprises hyaluronic acid or alpha-1-acid glycoprotein.
8. The corticosteroid conjugate of claim 5, wherein said synthetic polymer is a polyethylene glycol or N-hxg.
9. The corticosteroid conjugate of claim 1, wherein said charged group is a polyanion comprising at least three negatively charged moieties.
10. The corticosteroid conjugate of claim 1, wherein said charged group is a cation.
11. The corticosteroid conjugate of claim 1, wherein said bulky group comprises a corticosteroid.
12. A method of treating an autoimmune or inflammatory condition in a mammal, said method comprising administering to said mammal a corticosteroid conjugate of claim 1 in an amount effective to treat said condition.

13. The method of claim 12, wherein said condition is selected from the group consisting of asthma, psoriasis, eczema, organ/tissue transplant rejection, graft vs. host reactions, Raynaud's syndrome, autoimmune thyroiditis, Grave's disease, autoimmune hemolytic anemia, autoimmune thrombocytopenia purpura, mixed connective tissue disease, idiopathic Addison's disease, Sjogren's syndrome, urticaria, dermatitis, multiple sclerosis, rheumatoid arthritis, insulin-dependent diabetes mellitus, uveitis, Crohn's disease, ulcerative colitis, lupus, tendonitis, bursitis, adult respiratory distress syndrome, shock, oxygen toxicity, glomerulonephritis, vasculitis, reactive arthritis, necrotizing enterocolitis, Goodpasture's syndrome, hypersensitivity pneumonitis, glomerulonephritis; encephalomyelitis, and meningitis.

14. The method of claim 12, wherein said condition is rheumatoid arthritis or colitis.

15. The method of claim 12, wherein said corticosteroid conjugate is administered by intravenous, intraperitoneal, subcutaneous, ocular, topical, nasal, or intramuscular administration.

16. A method for inhibiting passage across the blood-brain barrier of a corticosteroid, said method comprising covalently attaching a group that is a bulky group of greater than 400 daltons or a charged group of less than 400 daltons, wherein said group increases the size, or alters the charge, of the corticosteroid sufficiently to inhibit passage across the blood-brain barrier without destroying the anti-inflammatory activity of said corticosteroid.

17. The method of claim 16, wherein said group is covalently linked via one or more of positions C16, C17, and C21 of said corticosteroid.

18. A pharmaceutical composition comprising an effective amount of a corticosteroid conjugate of claim 1, together with a pharmaceutically acceptable carrier or diluent.